

IN THE TITLE:

Please amend the title pursuant to 37 C.F.R. § 1.121 (see the accompanying "Marked-Up Version"):

① --POLYNUCLEOTIDES ENCODING PLASMODIUM VIVAX BLOOD STAGE ANTIGENS--.

REMARKS

Reconsideration of this application is respectfully requested.

In the Office Action, a Preliminary Amendment to the specification was objected to under 35 U.S.C. § 132 and claims 22 and 23 were rejected under 35 U.S.C. § 112, first and second paragraphs and 102(b). Claims 22 and 23 are pending in this application and are at issue.

The issues raised by the Examiner in the Office Action are summarized and addressed below.

In the Office Action, the Examiner implied that the application did not claim priority under 35 U.S.C. § 120 based on previously filed co-pending applications as she made the statement "If Applicant desires priority under 35 U.S.C. § 120 based upon a previously filed co-pending application, specific reference to the earlier-filed application must be made in the instant application.". Applicant respectfully submits that priority was claimed in this case in the transmittal papers filed with this continuation application on September 21, 2000. A copy of the transmittal papers as filed showing the claim to priority as a preliminary

amendment is appended hereto as Exhibit 1. This material has been added to the first page of the substitute specification (see below).

The drawings filed with this case were also objected to by the Examiner. Applicant has obtained and enclose herewith formal drawings which were prepared according to the Notice of Draftsperson's Patent Drawing Review, form PTO-948.

The Examiner also required the submission of a substitute specification, including any amendments and the claims required pursuant to 37 C.F.R. § 1.125(a). Enclosed herewith is a substitute specification appended hereto as Exhibit 2. Applicant respectfully submits that the substitute specification only contains subject matter from the original specification and any previously entered amendment under 37 C.F.R. § 1.121.

The Examiner also stated that the title of the invention was not descriptive and required a new title which was clearly indicative of the invention to which the claims are directed. Applicant has amended the title of the invention as required by the Examiner to read "Polynucleotides Encoding Plasmodium Vivax Blood Stage Antigens".

An Information Disclosure Statement, form PTO-1449 and the requisite fee is also enclosed herewith appended hereto as Exhibit 3.

The Examiner also objected to the Preliminary Amendment filed September 21, 2000 under 35 U.S.C. §132 because it allegedly introduced new matter into the disclosure. The added material which the Examiner alleged was not supported by the original disclosure was "EcoRI digest of purified . . . for tumors." which was inserted at page 5, line 18 after "1989". This was the definition of "stringent hybridization conditions" disclosed in Southern

et al. in J. Mol. Bio. 98:503, 1972. The Examiner alleged that the Southern et al. article did not (a) define "stringent conditions" and (b) one would not be directed to select the particular specific conditions as compared to any of the other numerous examples of specific hybridization conditions set forth by Southern et al. This objection is respectfully traversed and reconsideration respectfully requested.

Applicant respectfully submits that the amendment to the specification was proper and did not constitute new matter. In making this rejection, the Examiner has stated that Southern et al. describes multiple hybridization conditions, none of which are defined as "stringent hybridization conditions." This was addressed in the Declaration of Donald Crothers of record in this case. Dr. Crothers stated in paragraph 7 of his Declaration:

"... I conclude that a person of ordinary skill in the art, at the relevant time, would have recognized that all of the hybridization conditions as set forth in the Southern et al. publication are stringent hybridization conditions and that any set of the disclosed conditions would have resulted in selection of a hybrid between a nucleic acid of interest to an investigator and its complement.".

The Examiner has also stated multiple times that Southern et al. did not define any stringent hybridization conditions and did not define the particular conditions Applicant attempts to introduce as "stringent hybridization conditions." This was also addressed by the Crothers Declaration and it is stated on page 4:

The fact that the Southern publication does not refer to these hybridization conditions as stringent conditions is not an indication of lack of stringency. Although the term was known in 1972 at the time of the Southern publication, it was not in common use until after 1975. Nevertheless, the concept of

stringency i.e., the concept that the intrinsic specificity of the hybridization reaction depends on the annealing conditions employed, was familiar to those of ordinary skill in the field."

The Southern article has been incorporated by reference in its entirety. Therefore, these particular conditions, 65° C and 1X SSC salt concentration, acknowledged by Dr. Crothers as stringent, were a part of this application since the effective filing date of the parent application.

The Examiner has also stated that "Applicant has not addressed the section MPEP § 608.01(p) states that "Particular attention should be directed to the specific portions of the referenced document where the subject matter to be incorporated can be found." Applicant respectfully submits that this was addressed in the Preliminary Amendment filed on September 21, 2000 with this continuation application wherein it was stated "First, Applicant notes that 'the Manual of Patent Examining Procedures is merely a guide to the Examiner and is not controlling where it conflicts with the Statutes and Rules of Practice.' citing *Hawkins* 179 U.S.P.Q. at 160.

The case law clearly supports Applicant's position. Applicant has discussed the cited case law in their September 21, 2000 amendment, which is repeated here. The case law, including *In re Voss*, 194 USPQ 267 (CCPA 1973) and *In re Fouche*, 169 USPQ 429 (CCPA 1971), support the Applicant's position. The court *In re Voss* held that an earlier rejection, based on *In re Seversky* 474 F.2d 671, 177 USPQ 144 (CCPA 1973), confused

two different concepts: "(1) the right to have the benefit of the filing date of an earlier application under [35 USC §] 120 ... and (2) the incorporation by reference in an application of matter elsewhere written down (not necessarily in a patent application), for economy, amplification, or clarity of exposition ..." *Voss*, 194 USPQ at 270 (emphasis added). In the latter case of the situation where a reference incorporates material only for the purpose of economy, amplification or clarity, the court held that the incorporation of "Reference is made to United States Patent No. 2,920,971, granted to S.D. Stookey, for a general discussion of glass-ceramic materials and their production" was sufficiently specific without need for column and lines to allow later importation of material from the incorporated reference. *Voss*, 194 USPQ at 270.

Similarly, in *In re Fouche*, the court held that "identification was reasonably precise," even though the "appellant could have used a more precise identification technique ... [and] the technique used does not absolutely distinguish the application sought to be referenced from all other possible applications." *Fouche*, 169 USPQ at 431 (emphasis added). As in the above cases, Applicant referenced "stringent hybridization" conditions in Southern for the purposes of economy, amplification, or clarity of exposition. Therefore, like *In re Voss* and *In re Fouche*, and unlike a situation where reference is made in order to claim the benefit of an earlier filing date, Applicant in the present situation need not reference to a specific page or paragraph. As a result, *In re Voss* and *In re Fouche* are directly on point and Applicant's reference to Southern in the present specification has at least the same specificity.

Although Applicant respectfully submits that this is not necessary, Applicant also encloses herewith appended as Exhibit 4, a true copy of the original "Hawkins Declaration" filed during the prosecution of the parent application in order to make it part of this application as required by the Examiner. A proper "Hawkins" declaration was filed with this continuation application on September 21, 2000.

The Examiner has also misinterpreted the Crothers Declaration. The Examiner has taken the position that Dr. Crothers stated in his Declaration that stringent hybridization conditions in the Southern et al. article only apply to the hybrid duplex disclosed in the Southern et al. article and not to those in SEQ ID NO:1 of the instant application. Dr. Crothers made a statement that "It is generally found that this temperature occurs about 20° Celsius below the melting temperature of the hybrid duplex . . ." when referring to the temperature at which stringent hybridization occurs, and the Examiner stated that there was no indication of the melting temperature of the instantly claimed hybrid duplex. The Examiner concluded from the Declaration that the selection of stringent hybridization conditions was empirical in nature and not defined by the art. The Examiner also incorrectly stated that Dr. Crothers' Declaration emphasized the Examiner's position that stringent hybridization conditions are not art defined and are not defined in Southern et al. but are empirical in nature. Applicant respectfully disagrees with the Examiner. Stringent hybridization conditions are a combination of temperature and salt concentration. Thus, stringent hybridization conditions are disclosed in the Southern et al. article (e.g., 65°C, 1X SSC) and are not limited to the sequences disclosed therein. As the

temperature increases, increasing amount of salt (e.g., SSC) must be used. At 65° C, 1X SSC is used. At higher temperatures e.g., 80°C higher salt concentrations, 6X SSC, are used. Dr. Crothers stated this in his Declaration in paragraph 8 as follows:

"Southern used 65° C for hybridization in IX SSC, and showed the rate was maximum at 80° C for the higher salt concentration of 6X SSC as shown in Figure 5 of the Southern Publication." (emphasis added)

A key feature of stringent hybridization conditions that the Examiner apparently misunderstands is the function thereof. Two sequences hybridize (e.g., form a duplex) due to sequence similarity. Under stringent conditions, e.g., 65° C and 1X SCC salt concentration, only highly homologous sequences remain hybridized. Thus, the Examiner's statement on page 8 of the Office Action "Moreover, such a definition is necessarily a function of the hybrid duplex, because those that are less similar would have different melting temperatures and would therefore by definition have different 'stringent conditions' based upon Dr. Crothers' Declaration." Less similar sequences would not hybridize under stringent hybridization conditions. These are a measure of sequence similarity. Claims 22 and 23 are directed to nucleic acids hybridizable to SEQ ID NO:1 under stringent conditions and read on those sequences so alike SEQ ID NO:1 so as to hybridize under stringent conditions.

The Examiner also incorrectly stated that the Declaration of Dr. Crothers supports the lack of specific definition in the art for stringent hybridization conditions by referring to the incorporated hybridization conditions as "experimental" dependent upon melting temperature of the hybrid duplex and using the terms "generally" or "typically", not

"is" and "are". The Examiner has stated that if one went to the Southern et al. article for a definition of "stringent hybridization conditions" they would not find this term in the article. However, those of ordinary skill in the art in 1993 would recognize that all of the conditions in the Southern et al. article are stringent hybridization conditions.

Dr. Crothers has stated in paragraph 8 that:

"The fact that the Southern publication does not refer to these hybridization conditions as stringent conditions is not an indication of the lack of stringency." Although the term was known in 1972 at the time of the Southern publication, it was not in common use until after 1975. Nonetheless, the concept of stringency (i.e., the concept that the intrinsic specificity of the hybridization reaction depends on the annealing conditions employed), was familiar to those of ordinary skill in the field."

Dr. Crothers concluded in his declaration in the last sentence of paragraph 8:

"I am confident that, in 1993, a person of ordinary skill in the field would have recognized the hybridization conditions as disclosed in the Southern publication as what we would now call (and did call in 1993) stringent conditions."

This does not support the Examiner's position.

The Examiner mentioned that Dr. Crothers stated that a second important feature of stringent conditions is the importance of the wash period at the hybridization temperature. The Examiner noted that this important feature of "stringent hybridization" was not set forth in the claims, alleging that Applicant appeared to pick and choose elements of hybridization protocols. This is not the case. Those of ordinary skill in the art realize that the wash period is a part of the Southern hybridization assay. This is set forth on page 508 of the Souther et al. paper. When performing the Southern hybridization

assay, a separated, immobilized nucleic acid is hybridized with a second nucleic acid in solution under stringent hybridization conditions, i.e., 65° C in 1X SCC buffer. The solution is removed and the immobilized nucleic acid is washed with 1X SCC at 65° C to remove non-specifically bound material. Because the hybridization and the wash are conducted at the same salt concentration and temperature, they are both considered part of the same assay.

Therefore, Applicant respectfully submits that the objection to the specification under 35 U.S.C. § 132 is not well taken and should be withdrawn.

Claims 22 and 23 were also provisionally rejected under the judicially created Doctrine of Obviousness-Type Double Patenting as being unpatentable over claims 22, 26 and 28 of co-pending Application No. 08/719,821. Because this a provisional rejection, Applicant will submit a Terminal Disclaimer upon the indication of allowable subject matter in either this or the co-pending Application No. 08/719,821.

Claim 23 was rejected under 35 U.S.C. § 112, first paragraph, as the Examiner contended that it contained subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention. The Examiner contended that the recitation of "under hybridization conditions of 1X SCC at 65° C" was based on the amendment of the specification which has support only from the incorporation of new matter into the specification as set forth above. The Examiner concluded that it was not clear that Applicant had, at the time of the invention, conceived of

these particular hybridization conditions and therefore it was not clear that Applicant was in possession of the claimed invention at the time of filing. This rejection is respectfully traversed and reconsideration respectfully requested.

Applicant respectfully submits that based on the arguments above, that the amendment to the specification was proper and did not constitute new matter. The Southern et al. article was incorporated by reference in its entirety since the filing date of the parent application in this case i.e., 1993. Therefore Applicant was in possession of the claimed inventions since the filing of the parent application.

Therefore, Applicant respectfully submits that the rejection of claim 22 under 35 U.S.C. § 112, first paragraph, was not well taken and should be withdrawn.

Claim 22 is also rejection under 35 U.S.C. § 112, second paragraph, as being indefinite due to its recitation of "stringent conditions". The Examiner contended that "stringent conditions" was vague and indefinite, since no particular conditions were defined in the specification. This rejection is respectfully traversed and reconsideration respectfully requested.

This is the same issue as the new matter objection to the specification. Applicant respectfully submits that incorporation of the stringent hybridization conditions into the specification was proper and therefore the particular conditions in claim 22 are fully supported by the specification.

Therefore, Applicant respectfully submits that the rejection of claim 22 under 35 U.S.C. § 112, second paragraph, is not well taken and should be withdrawn.

Claims 22 and 23 were also rejected under 35 U.S.C. § 102(b) as being anticipated by Sigma Molecular Biology Product Guide, 1991, pages 54-56. The Examiner contended that the reference teaches isolated purified oligo-d(pA) and oligo-d(pT) oligonucleotides and that each of the oligonucleotide products share a 100% identity with at least resolutes 193-221 of SEQ ID NO:1. The Examiner concludes that these nucleic acids would hybridize under stringent conditions. This rejection is respectfully traversed and reconsideration is respectfully requested.

Applicant respectfully submits that the position that the Examiner is taking here is incompatible with her arguments above in the new matter objection and the Section 112, first and second paragraph rejections above, and supports Applicant's position. In making a rejection under Section 102(b), all of the limitations of the claim must be present in the reference. There is no disclosure in the Sigma reference to stringent or any hybridization conditions whatsoever.

There is no indication in the Sigma reference that the 28-long oligonucleotides of the reference would hybridize to SEQ ID NO:1 at 65° and 1 X SSC salt concentration set forth in claims 22 and 23 herein. These short oligonucleotides are outside the scope of claims 22 and 23 of the above-identified application.

Therefore, Applicant respectfully submits that the rejection of claims 22 and 23 under 35 U.S.C. § 102(b) is not well taken and should be withdrawn.

CONCLUSION

Claims 22 and 23 are in a condition for allowance.

In view of the above amendments and remarks, reconsideration of this application and issuance of a Notice of Allowance for this application is respectfully requested.

Respectfully submitted,



Howard M. Frankfort, Ph.D.
Reg. No. 32,613
Agent for Applicants

DARBY & DARBY, P.C.
Post Office Box 5257
New York, NY 10150-5257
Phone (212) 527-7700

**ATTACHMENT: MARKED-UP VERSION IN CONFORMANCE WITH
37 C.F.R. 1.121 FOR AMENDMENT OF JANUARY 2, 2002**

IN THE TITLE:

Please amend the title pursuant to 37 C.F.R. § 1.121 (see the accompanying "Marked-Up Version"):

**POLYNUCLEOTIDES ENCODING PLASMODIUM VIVAX BLOOD STAGE
ANTIGENS[, ANTIBODIES AND DIAGNOSTIC ASSAYS]**

Howard M. Frankfort

Patent Agent for Applicant

Pending Claims

22. An isolated and purified nucleic acid hybridizable to polynucleotide of SEQ ID NO. 1, under stringent conditions.
23. The isolated and purified nucleic acid of claim 22, wherein said stringent conditions are 1X SSC at 65°C.